Remarks

A restriction requirement under 35 U.S.C. §§121 and 372 was set forth in the Official Action dated February 23, 2007 in the above-identified patent application.

At the outset, it is noted that a shortened statutory response period of one (1) month was set forth in the February 23, 2007, 2006 Official Action. Therefore, the initial due date for response was March 23, 2007. A petition for a two (2) month extension of time is presented with this response, which is being filed within the two month extension period.

It is the Examiner's position that claims 1-38 and 42-44 in the present application are now drawn to ten (10) patentably distinct inventions which are as follows:

Group I: Claim(s) 1-8 drawn to DNA encoding $p66^{shc}$ with altered serine residues, vector and host cell containing it and the polypeptide encoded thereby, the method of making the protein product;

Group II: Claim(s) 9-11, drawn to method of modulating resistance in cells to oxidative stress comprising contacting said cell with an agent capable of modulating $p66^{shc}$ gene expression;

Group III: Claim(s) 12-21, drawn to a method of increasing resistance in cells to oxidative stress comprising disrupting the $p66^{shc}$ signaling pathway;

Group IV: Claim(s) 22-27 drawn to a method for increasing resistance in cells to oxidative stress comprising administration of an effective amount of an agent which disrupts $p66^{shc}$ or a step in the $p66^{shc}$ signaling pathway;

Group V: Claim(s) 28-31 drawn to a method of increasing resistance to tumor formation comprising the step of increasing the expression of $p66^{shc}$;

Group VI: Claim 32-35 drawn to a method of screening for compounds capable of modulating resistance in

cells to oxidative stress by modulating a $p66^{shc}$ signaling pathway;

Group VII: Claim(s) 36-38 drawn to a method of reducing intracellular levels of reactive oxygen species in a cell by contacting with an agent capable of inhibiting the expression of the activity of $p66^{shc}$;

Group VIII: Claim 42 drawn to a method of determining the presence or absence of an unaltered $p66^{shc}$ nucleic acid by contacting with a specifically hybridizing nucleic acid;

Group IX: Claim 43 drawn to a method of determining the presence or absence of an unaltered $p66^{shc}$ by contacting with an antibody binding domain; and

Group X: Claim 44 drawn to an expression system comprising a nucleic acid vector having an unaltered p66shc coding sequence.

The Examiner further contends that Groups III, IV and VII encompass patentably distinct species and if any of these groups are elected, the Examiner has required applicants to elect a single species from these groups for examination on the merits. Following such an election, Applicants must also indicate which claims read on the elected species.

At the outset, Applicants are dismayed that the Examiner has chosen to restrict the present application further despite Applicants strenuous traversal of the initial requirement for restriction. Applicants continue to respectfully disagree with the Examiner's position and submit that a withdrawal, or at the very least a modification of the instant restriction requirement is clearly in order for the following reasons.

First, it is the Examiner's position that the inventions listed as Groups I - X do not relate to a single general inventive concept under PCT Rule 13.1, because, under PCT Rule 13.2, they lack the same or corresponding special technical feature. Applicants respectfully submit that the Examiner's approach to unity is incorrect. The only requirement for

unity of invention is whether there is a single general inventive concept to the claims. A single general inventive concept will exist where there is the same or corresponding special technical feature. This is apparent from the fact that that only requirement set out in the Rules of the PCT governing how unity is assessed is Rule 13 PCT. Rule 13 PCT states that:

> 13.1 Requirement:
>
> The international application shall relate to one invention only or to a group of inventions so linked as to form a single general inventive concept ("requirement of unity of invention").
>
> 13.2 Circumstances in Which the Requirement of Unity of Invention Is to Be Considered Fulfilled:
>
> Where a group of inventions is claimed in one and the same international application, the requirement of unity of invention referred to in Rule 13.1 shall be fulfilled only when there is a technical relationship among those inventions involving one or more of the same or corresponding special technical features. The expression "special technical features" shall mean those technical features that define a contribution which each of the claimed inventions, considered as a whole, makes over the prior art.

Accordingly, the MPEP section 1893.39(d) states that: "When making a lack of unity of invention requirement, the examiner must (1) list the different groups of claims and (2) explain why each group lacks unity with each other group (i.e., why there is no single general inventive concept) specifically describing the unique special technical feature

in each group."

Thus, the MPEP specifically requires the Examiner, when making a lack of unity requirement, to explain why there is no single general inventive concept. In the present case, the Examiner has acknowledged the presence of a special corresponding technical feature and hence a single inventive concept. Therefore, Applicants respectfully submit that there is no basis for finding a lack of unity under the MPEP.

Additionally, Applicants respectfully submit that during the international stage of this application the PCT Examiner did not make a lack of unity finding and considered all of the claims to be directed to a single invention. Plainly, the instant restriction requirement fails to comply with the established United States Patent and Trademark Office practice of following the international rules regarding unity of invention in the prosecution of applications filed under §371. While the Examiner purports to employ the general inventive concept practice under PCT Rule 13.1, it is wholly unclear how the Examiner could conclude that the instant application has ten (10) Groups of inventions, when the PCT Examiner, employing the same rules, determined that identical claims in the international application have **complete unity** of invention. Accordingly, Applicants respectfully request the instant restriction requirement be withdrawn and all of the claims be examined on their merits.

The present invention relates to the inventive concept that $p66^{shc}$ acts in a pathway that regulates stress response. This was not recognized anywhere in the art and constitutes a significant contribution to the art.

Claims 1-8 (Group I) relate to a mutated version of $p66^{shc}$ having reduced potential for serine phosphorylation and hence reduced participation in the stress response pathway. The claims of group II, e.g., claims 9-11 relate to methods of modulating the stress response pathway by modulating the

recited $p66^{shc}$ signaling pathway. Increased resistance to oxidative stress, increased resistance to tumor formation, and reduced intracellular levels of reactive oxygen species (ROS) are all outcomes of a modulated stress response. Inasmuch as claim 9 reads on a method of modulating resistance to oxidative stress in cells by modulating p66 gene expression, Applicants submit that placement of claims 12-21 and 22-27 in separate groups of invention is wholly improper. Clearly, claim 9 is generic to the Groups II and IV inventions at the very least. Group III is directed to a method of increasing (e.g., modulating as in claim 9) resistance to oxidative stress by disrupting p66 signaling pathway while claims 22-27 are drawn to a comparable method wherein an agent is employed to disrupt the $p66^{shc}$ signaling pathway. It cannot be reasonably maintained that a proper search of any of the Group II, III or IVs invention would not be co-extensive. Applicants also submit that such a search would encompass the claims of the Group VI invention, namely claims 32-35, as amended herein, which are directed to methods of screening for compounds capable of modulating resistance in cells to oxidative stress by modulating a $p66^{shc}$ signaling pathway. Clearly, a proper search of the foregoing Groups of claims does not impose an increased search burden on the Examiner

Thus, at least the claims of Groups II, III, IV and VII invention clearly relate to the same inventive concept, i.e., the participation of $p66^{shc}$ in a pathway that regulates stress response. Accordingly, Applicants respectfully request withdrawal of the restriction requirement between these claims. Indeed, all of claims 9-11, 12-27 and 32-35, and 45-52 expressly refer to methods of <u>modulating resistance in cells to oxidative stress by modulating the $p66^{shc}$ signal transduction pathway</u>, or to methods of screening for compounds which <u>modulate resistance in cells to oxidative stress by modulating the $p66^{shc}$ signal transduction pathway</u>.

Support for the amendments can be found throughout the specification including, for example, page 12, line 8-12 as well as in the original claims as filed. New claims 45-52 have been added which depend directly or indirectly from claim 9. The Examiner is respectfully requested to place these new claims in the Group II invention as these claims cannot be considered **independent** and distinct from the Group II invention as this group includes claim 9. Support for the new claims can be found in the claims as originally filed and at page 19, lines 25-30.

Thus, at the very least, Applicants submit that the pending claims must be considered to relate to a common inventive concept (namely, the involvement of $p66^{shc}$ in the oxidative stress response pathway). Accordingly, Applicants request that the restriction requirement be withdrawn between the groups II, III, IV and VII inventions at the very least.

In order to be fully responsive to the instant restriction requirement, Applicants hereby elect, with traverse, Group II, namely claims 9-11 and new claims 45-52 drawn to a method of increasing resistance in cells to oxidative stress.

Applicants' election in response to the present restriction requirement is without prejudice to their right to file one or more continuing applications, as provided in 35 U.S.C. §120, on the subject matter of any claims finally held withdrawn from consideration in this application.

The Examiner has objected to claims 1, 2, 5-8, 12, 13, 17, 32 and 43 as containing minor informalities. These informalities have been rectified in accordance with the present amendment, thereby rendering this object moot.

At page 10 of the Restriction Requirement, the Examiner contends that the application is not in compliance with the sequence listing rules. Submitted herewith is a paper copy and computer readable form of the sequence listing

which has been amended to list codons encoded by SEQ ID NO: 1. The undersigned verifies that the paper copy and CRF forms of the sequence listing are identical to those initially filed in the application and do not contain new matter. Entry of the amended sequence listing in to the application is respectfully requested.

Early and favorable action on the merits of this application is earnestly solicited.

Respectfully submitted,
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